EXHIBIT C

Expert Report of Marc R. Toglia, M.D.

I. Qualifications

I am a sub-specialist in the field of Female Pelvic Medicine and Reconstructive Pelvic Surgery. I am double board certified in Female Pelvic Medicine and Reconstructive Surgery (2012) and Obstetrics and Gynecology (1995) and am licensed to practice medicine in Pennsylvania. Currently I serve as the Chief of Female Pelvic Medicine and Reconstructive Surgery for the Main Line Health System in suburban Philadelphia. I also hold the academic title of Associate Professor of Obstetrics and Gynecology at Thomas Jefferson School of Medicine and Associate Clinical Professor at the Lankenau Institute of Medical Research (LIMR).

I received my Doctor of Medicine from Vanderbilt University School of Medicine in 1989, and completed an Obstetrics and Gynecology residency at the University of Michigan Medical Center in 1993. During my residency, I trained under renowned urogynecologist Dr. John Delancey and the urologist Edward McGuire, MD, a pioneer in the development of sling surgery for women. During both my undergraduate and graduate career, I was actively involved in both basic science and clinical research at Duke University Medical Center, the Howard Hughes Medical of Molecular Biology at Vanderbilt University and Vanderbilt University Medical Center.

After graduating from residency, I accepted a position as assistant professor of Obstetrics and Gynecology at the State University of New York at Stony Brook, where I helped to establish the division of Urogynecology with Andrew Fantl, MD and Joseph Schaffer, MD, two other notable urogynecologists. In 1996, I moved to Philadelphia, where I established the Division of Urogynecology at the Main Line Health System in suburban Philadelphia. I maintain a busy clinical practice, performing approximately 200 vaginal reconstructive and/or incontinence procedures a year, oversee the residency training in Female Pelvic Medicine at the Lankenau Medical Center, and serve as an associate clinical researcher at the Lankenau Institute of Medical research.

I am an internationally recognized expert in the field of Urogynecology. I currently serve as an editor for the two premier Urogynecology medical journals -- Female Pelvic Medicine & Reconstructive Surgery (FPMRS) and the International Urogynecology Journal (IUJ), and serve active leadership roles in the American Urogynecologic Society and the Society for Gynecologic Surgeons.

I have over 34 years of experience in clinical and basic science research. I have published numerous scholarly articles within the field of medicine since 1984 on a wide range on subjects. Additionally, I have authored numerous medical textbook chapters and I am a co-author of the textbook Office Urogynecology. I have published scholarly articles concerning gynecology, urogynecology and urinary incontinence in many of our premier medical journals including the New England Journal of Medicine, American Journal of Obstetrics and Gynecology, Obstetrics and Gynecology, IUJ and FPMRS. My clinical research has included authorship of a randomized clinical trial comparing the retropubic TVT with a third generation sling, as well as a retrospective cohort examining complications with native tissue repairs with permanent sutures for vaginal reconstruction. These studies have been presented at both national and international scientific meetings.

Throughout my career, I have performed thousands of gynecologic surgeries, specifically female pelvic floor reconstruction, such as abdominal sacral colpopexy, vaginal approaches including vaginal hysterectomy, high uterosacral suspensions, sacrospinous ligament suspensions, native tissue repair, biologic graft and synthetic mesh augmented repairs. I was trained to perform retropubic colposuspensions by Drs. John Delancey and Andrew Fantl, and autologous fascial pubovaginal slings by Dr. Edward McGuire. I was trained to perform vaginal pelvic reconstruction repairs by Drs. John Delancey and Andrew Fantl. I am considered one of the leading experts in the greater Philadelphia region on surgical revision of complications related to female pelvic floor reconstruction including native tissue and abdominal and vaginal mesh procedures.

During my career, I have developed extensive experience with a variety of polypropylene mesh products designed for surgical use in the female pelvic floor. I began performing the Gynecare TVT procedure in 1999, shortly after it was introduced in the United States. Since then I have performed over 2,500 mid urethral sling procedures in my current practice including the retropubic approach (TVT, TVT Exact), transobturator approach (TVT-O, TVT abbrevo) and single incision slings such as the TVT Secur. I have performed vaginal and abdominal mesh and mesh augmented repairs for the treatment of pelvic organ prolapse including freehand cut Gynemesh PS for mesh augmentation vaginally, use of the Prolift device, and I have also performed abdominal sacral colpopexy. I have been formally trained on all of these procedures.

I have actively participated in the Ethicon Professional Education for these products and have trained other surgeons, including Urogynecologists, Urologists, and Gynecologists from around the country. I have served as faculty in a wide range of professional educational activities, including invited lectures, cadaver labs, as well as proctoring and preceptorships. I have also consulted on the design and the analysis of other prototype procedures.

For additional information please refer to my attached Curriculum Vitae.

II. Materials Reviewed

In preparation of my opinions I have searched and reviewed the medical and scientific literature through Medline and Cochrane databases and bibliography searches of studies regarding pelvic organ prolapse surgical repairs, including studies of transvaginal repair that compared native tissue repair to repairs using grafts or mesh. I have also incorporated my personal surgical experience over the past 24 years and information gathered at national and international scientific meetings that I attended during this time period. I have also reviewed the Ethicon Gynemesh PS and Prolift Instructions for Use, Professional Education materials made available to users of Prolift (pelvic floor surgeons), Prolift Surgeons Resource Monograph, and other Ethicon documents. A list of these materials and those that I may use at trial are attached to this report. I have also reviewed the Plaintiffs' expert reports and the materials cited by Plaintiffs' experts.

III. Fees and Expert Testimony

My fees for serving as an expert in this matter are: $400/hour for review, report drafting and meetings and $4,000/day for deposition and trial testimony. I have given expert deposition testimony in the prior four years in the Mullins v. Ethicon TVT case on October 2, 2015.

IV. Opinions

What follows are my opinions and the bases for the opinions. They are based on my education, training, professional experience, clinical research and teaching I have performed, my review of the medical and scientific literature, as well as my experience as an editor for the leading medical journals in my field. They are also

a reflection of my annual participation in the annual scientific meetings of national and international medical societies since 1993, including the published Position Statements and Systematic Review Guidelines of these societies. All of my opinions are held to a reasonable degree of medical and scientific certainty. In summary, in my opinion, the Gynemesh PS and Prolift are safe and effective, leading to significant anatomic, subjective and quality of life improvements while having an acceptable complication profile with risks that are similar to native tissue repair and suspension procedures such as dyspareunia, pelvic pain, change in vaginal dimensions, scarring and wound complications, and the design is reasonably safe for its intended use as discussed below. Moreover, the risks of use of the device are adequately set forth to pelvic surgeons in the IFU, professional materials, Prolift Surgeons Resource Monograph, and are elemental risks that occur with pelvic organ prolapse surgery and are expected to be known by pelvic floor surgeons due to their education, professional training and knowledge of basic risks and the medical literature.

A. Background

Pelvic organ prolapse (POP) is a common and bothersome condition that significantly degrades a woman's quality of life, including daily functions such as bowel and bladder emptying, sexuality, body image and social interactions. It is a highly prevalent condition in the United States, currently affecting 3.3 million women (Wu et al Obstet Gynecol 2009; 114:1278–83) and represents a major public health issue in the United States. The prevalence of this condition is expected to increase by 46% in the United States to 4.9 million women by 2050 (same reference).

Pelvic organ prolapse describes a group of pelvic floor disorders affecting women in which the pelvic organs, including the uterus, bladder or bowel become displaced anatomically, and protrude into or beyond the vagina, due to weakness in the tissues that normally support these organs. POP is associated with a wide range of bothersome symptoms including bladder and bowel dysfunction, such as incontinence or difficulty with evacuation, as well as discomfort, pain and sexual dysfunction.

It is well established that women who suffer from pelvic floor disorders such as stress urinary incontinence and pelvic organ prolapse have weakened or structurally altered connective tissue, including deficiencies in their collagen matrix (Norton P et al, 1992; Ulmsten 1987; Gilpin 1989; Cosson et al, 2003). As a result, many women can present with prolapse at multiple compartments. Risk

factors for prolapse include pregnancy, childbirth, congenital or acquired connective tissue abnormalities, denervation or weakness of the pelvic floor, aging, hysterectomy, menopause and factors associated with chronically raised intra-abdominal pressure such as heavy lifting, chronic cough from smoking and COPD (Bump 1998; Gill 1998; MacLennan 2000).

POP is common and can be seen on examination in 40%to 60% of parous women (Handa 2004; Hendrix 2002). Of these, it has been reported that about 12 % are symptomatic (Slieker-ten Hove 2009 Int Urogynecol J Pelvic Floor Dysfunct 20(9):1013–1021). Symptoms of prolapse include pelvic heaviness, a sense of a bulge, lump or protrusion coming down from the vagina, a dragging sensation in the vagina, or backache and symptoms of bladder, bowel or sexual dysfunction are frequently present. (Maher 2013)

Women with symptomatic prolapse suffer physical and emotional distress (Subak 2001 Obstet Gynecol 98(4):646–651) which has a significant negative impact on women's social, physical, and psychological wellbeing (Abdel-Fattah 2011 BMJ Open 1(2):e000206. doi:10.1136/ bmjopen-2011-000206). As the general population ages, pelvic floor dysfunction will become increasingly burdensome in terms of reduced quality of life, workforce productivity, and cost to both the individual and the health care system as a whole (Wu 2009 Obstet Gynecol 114(6):1278–1283). Many women with POP report concomitant SUI and in women with stage II POP, about 55% also have SUI (Maher 2013). Occult SUI, also referred to as hidden or masked SUI, is common in women with POP and has been found in up to 65% of women following prolapse reduction (Reena 2007).

B. Surgical Treatment of Pelvic Organ Prolapse.

Pelvic organ prolapse is a highly prevalent condition that is often managed surgically. Surgical approaches are typically based upon the severity of the prolapse and associated symptoms, as well as the woman's general health and surgeon preference and experience.

A commonly referenced statistic is that the lifetime risk that a woman will undergo a single operation for incontinence or prolapse is 11.1% (Olsen 1997). More contemporary, population based analysis have found that lifetime risk of pelvic organ prolapse surgery to be 12.6% in the United States (Wu et al Obstet Gynecol 2014; 123:1201–6) and a cross sectional study from Australia reported a rate of 19% (Smith et al, Obstet Gynecol 2010;116:1096-100). Estimates show that

approximately 220,000 surgeries are performed annually in the United States for pelvic organ prolapse (Brown JS, et al. Am J Obstet Gynecol 2002;186:712–6). In comparison, a woman's lifetime risk of developing breast cancer is 14.8%

The surgical approach to pelvic organ prolapse remains a significant challenge. The route and types of surgery vary widely, depending on the type of prolapse and the associated symptoms. Furthermore, the impact of surgery on bowel, bladder and sexual function can be unpredictable and may make symptoms worse, or result in new symptoms such as leakage of urine or problems with sexual intercourse (Cochrane 2007).

The goal of prolapse surgery is to restore normal vaginal anatomy and support, and restore or maintain normal bladder, bowel, and vaginal (eg sexual) function. The gynecologic surgeon must choose from a wide variety of abdominal or vaginal approaches, or a combination of these approaches. In addition, the surgeon must decide whether to use absorbable or permanent sutures to achieve these goals or rely upon synthetic mesh material or biologic grafts

Traditional surgical approaches for pelvic organ prolapse include vaginal incisions and suture based repairs, (eg native tissue plications). However, anatomic recurrence has been common, with almost 30% of women requiring a repeat procedure (Olsen 1997). Others have reported the prevalence of reoperation after a primary pelvic reconstructive surgery to be 43%-58% (Clark AL et al. Am J Obstet Gynecol. 2003; 189(5):1261–1267; Whiteside JL et al. Am J Obstet Gynecol. 2004; 191(5):1533–1538). It was widely held in the 1990's that the risk of re-operation for pelvic organ prolapse following a traditional vaginal approach was as high as 30% - 50%.

Randomized clinical trials, and longitudinal cohort studies from the 1990's suggested that surgical approaches using synthetic mesh placed abdominally result in better outcomes compared with traditional native tissue plication performed vaginally (Benson et al. 1996). In an attempt to address the significant recurrence rates associated with traditional vaginal repair methods, gynecologic surgeons, both in the United States and abroad began investigating newer techniques of vaginal repair with biologic grafts and synthetic mesh implants. In 2002, Gynemesh PS was approved by the United States Food and Drug Administration for prolapse repair and in 2004, transvaginal synthetic mesh kits were approved by the United States Food and Drug Administration.

C. Use of Surgical Mesh in Female Pelvic Reconstruction Before Prolift.

The rationale for use of mesh is based upon a hypothetical reduction of the high recurrence rates after standard vaginal surgery without mesh, as well as the observation that pelvic organ prolapse occurs in women with deficient support tissues and markedly weakened pelvic floor musculature – two conditions that cannot be addressed by simple suture plication.

Surgical mesh has been used since the 1950s for abdominal hernia repair. There is a long history of the use of synthetic grafts in pelvic reconstruction surgery in light of the high rates of recurrence with existing native tissue procedures (Moore et al, 1955; Weber et al, 2001; Sand et al, 2001; Whiteside et al, 2004; Nguyen et al, 2008). Moore et al reported on the use of tantalum mesh cut in a trapezoidal shape, placed transvaginally, and anchored posteriorly to the cardinal ligaments and anteriorly to the periosteum of the median surface of the pubic rami for the treatment of cystoceles. Dissatisfied with high recurrence and complications such as impairment of vaginal function, pain, and marked shortening of the vagina with existing vault repairs, Lane described a procedure utilizing a synthetic graft attached to the vaginal vault and secured to the sacrum via the anterior longitudinal ligament (Lane 1962). The use of synthetic mesh slings for treatment of incontinence was well described in the 1970s and 1980s. (Morgan 1970; Nichols DH 1973; Stanton 1985). The use of various synthetic materials to treat prolapse continued in the 1970s to 1990s with efficacy and complications reported in the medical literature (Iglesia et al, 1997).

The use of mesh by gynecologic surgeons for the treatment of SUI and POP became commonplace in the 1990's. Clinical trials highlighted the high success rates of abdominal pelvic organ prolapse repair (eg sacral colpopexy) and the growing success and popularity of SUI surgeries based upon polypropylene mid-urethral synthetic mesh slings.

In 1996, the results of a long term prospective randomized controlled trial of vaginal versus abdominal prolapse surgery was published (Benson et al, 1996). 88 women with uterovaginal or vaginal vault prolapse were randomized and 80 (vaginal 42, abdominal 38) were available for evaluation at a mean follow up of 2.5 years (range 1 – 5.5 years). In the vaginal group, the women underwent bilateral sacrospinous ligament vault suspension and vaginal paravaginal repair with permanent monofilament suture. In the abdominal group, the women underwent sacral colposuspension and an abdominal paravaginal repair with permanent monofilament suture. Both groups underwent additional concomitant

procedures as needed. Surgical effectiveness was optimal in 29% of the vaginal group and 58% of the abdominal group and was unsatisfactory leading to reoperation in 33% of the vaginal group and 16% of the abdominal group. Reoperations were most common for recurrent cystocele, 12 from the vaginal group (29%) and 4 from the abdominal group (10.5%). Vaginal vault inversion recurred in 5 from the vaginal group (12%) and 1 from the abdominal group (2.6%). The relative risk of an unsatisfactory outcome by the vaginal route was 2.11 (95% confidence interval 0.90 – 4.94)

The first Cochrane review on the surgical management of pelvic organ prolapse in women, published in 2007, supported the conclusion that an abdominal sacral colpopexy resulted in superior anatomic and functional results compared to traditional vaginal repairs with native tissue plication (Cochrane 2007). This conclusion was based upon a review of 22 surgical trials involving 2368 women. The Cochrane review concluded that recurrence rates of pelvic organ prolapse were significantly lower with abdominal sacral colpopexy compared to vaginal approaches, and additionally were associated with less postoperative dyspareunia, post-operative stress urinary incontinence, and a lower rate of reoperation. This systematic review included an analysis of three RCTS comparing abdominal sacral colpopexy versus vaginal sacrospinous vault suspension ((Benson 1996; Lo 1998; Maher 2004). In all three trials, abdominal sacral colpopexy was better than the vaginal approach in terms of a lower rate of recurrent vaginal vault prolapse, the number of women failing to improve to Stage 2 POP or better and a lower reoperation rate for prolapse.

The use of mesh in a vaginal surgical approach for prolapse repair has been suggested since Julian et al found in a non-randomized prospective study that in women who had undergone at least two previous vaginal repairs, the overlaying of a Marlex (Bard) mesh to the anterior vaginal wall repair was associated with lower recurrence rates of cystocele from 33% to 0% (Julian 1996). The Marlex mesh was associated with a mesh erosion rate of 25% (Julian 1996). Flood et al, in a retrospective review of 142 women with Marlex mesh augmentation of anterior vaginal wall repair, reported a 100% success rate for cystoceles at 3.2 years and a mesh erosion rate of only 2% (Flood 1998).

The TVT device, which uses a macroporous Prolene polypropylene knitted mesh, was introduced in 1998 and has revolutionized the field of stress urinary incontinence. It was developed over a long period of intense study. (Petros 1990, 1993). The earliest prototypes for the TVT device critically evaluated the use of a variety of synthetic materials, such as Mersilene and Gortex before the Prolene

polypropylene mesh found higher exposure rates (Ulmsten et al, 1996; Petros 2015). These authors also reported that these materials (Gore-Tex, Teflon, Mersilene) were associated with significant inflammatory reaction in paraurethral tissues and caused a significant amount of tape rejection. (Falconer et al, 2001). Conversely they reported minimal to no inflammatory reaction with the macroporous Prolene polypropylene mesh and no rejection.

Pore size affects the inflammatory response and resultant connective tissue formation within and into the mesh, and the rearrangement of materials such as collagen within the mesh structure. Macroporous meshes (pore size in excess of 75 μm) easily allow macrophages, leukocytes, fibroblasts, blood vessels and collagen to transverse the pores: thus macroporous meshes promote tissue host ingrowth with resultant biocompatibility and low risk of infection (Amid 1997).

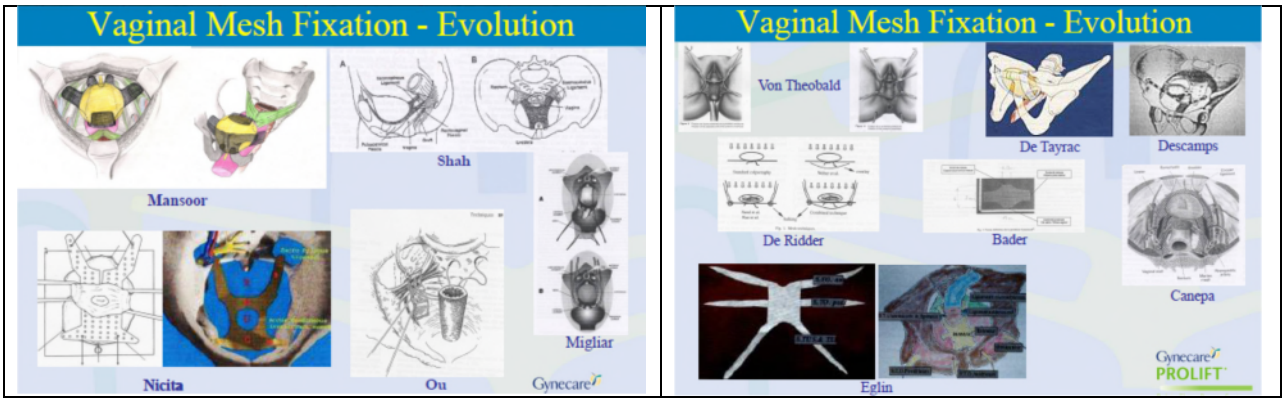
Polypropylene material has been widely considered safe and effective as a surgical implant for over five decades, and has been used in a majority of surgical specialties including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology and urology. Polypropylene is associated with a more vigorous connective tissue reaction than absorbable materials, which increases repair strength and generates better scar formation. In 2002, Gynemesh PS received FDA approval for pelvic reconstructive surgery. As an isolated thread, it is used widely as a permanent and durable surgical suture. As a knitted material, polypropylene mesh is the consensus graft material in a number of areas in the human body. Within the field of Female Pelvic Medicine, the use of knitted polypropylene, in the form of a macroporous, monofilament, light weight mesh tape has demonstrated long term durability, safety and efficacy up to 17 years (Nilsson et al. IUJ 2013; AUGS-SUFU Position Statement on Mesh Midurethral Slings for SUI 2014).

Specifically, type 1 polypropylene mesh is universally recognized as possessing the highest biocompatibility with the least propensity for infection. (Ford Cochrane Review 2015). Macroporous mesh allows for entry of fibroblasts, macrophages, blood vessels and collagen fibers, thus minimizing the risk of infection and optimizing collagen infiltration and decrease in flexural rigidity. In contrast, microporous mesh results in restriction in fibroblast infiltration which can result in encapsulation. I have personally used Gynemesh PS and related materials as my primary implant material in my patients for over 15 years in more than 3,000 patients, and have yet to observe a single case of mesh rejection, clinically significant foreign body reaction, mesh encapsulation or infection.

Subsequent clinical trials demonstrated the safety and appropriateness of using the macroporous type 1 Prolene polypropylene mesh in TVT (Rezapour & Ulmsten, 2001; Rezapour et al, 2001; Nilsson et al, 2001). By 2001, over 100,000 TVT procedures had been performed worldwide. Data on TVT continued to be published that confirmed the utility, efficacy and safety of the macroporous type 1 Prolene polypropylene mesh as earlier reported. There currently are studies with 5, 10, and 17 years clinical follow up with the macroporous Prolene polypropylene mesh that document the safety of vaginal placement of the material. (Liapis et al, 2008; Nilsson et al, 2008, 2013; Olsson et al, 2010; Groutz et al, 2011; Heinonen et al, 2012; Serati et al, 2012; Svenningsen et al, 2013; Laurikainen et al, 2014; Tommaselli et al, 2015).

Besides the high failure rates with native tissue prolapse repair, another movement was afoot in the field of female pelvic medicine that led to the development of Gynemesh PS and Prolift. The abdominal sacral colpopexy, while an effective procedure, was considerably more invasive and morbid. The abdominal route often resulted in wound infections, herniations, seroma and wound complications, as well as undesirable scarring, pain and nerve injury. The abdominal approach also has a higher risk of small bowel ileus, and obstruction, surgical hemorrhage, and risk of venous thromboembolism As a result, there was a need for a design to reduce these complications by utilizing a vaginal approach. This is analogous and contemporaneous with the trend towards less invasive approaches in gynecologic surgery, away from abdominal hysterectomy, towards endoscopic and vaginal hysterectomy.

The gaining popularity of transvaginal mesh implants in the 1990s and beyond, both in the United States and beyond, was supported by a growing body of scientific literature supporting their efficacy (Watson et al, 1996; Julian 1996; Flood et al, 1998; Nicita 1998; Hardiman et al, 2000; Sand et al, 2001). A variety of approaches and techniques were described, as well as differences in mesh configuration as surgeons were cutting sheets of mesh to shape:



However, it was not until the work of the TVM Group that a standardized, reproducible technique and device was developed and assessed.

D. Gynemesh PS and Prolift.

Based upon the success of the TVT procedure, attributed to the use of a macroporous monofilament mesh coupled with a standardized and reproducible technique, a group of physicians formed the TVM group to address the limitations of traditional vaginal approaches to pelvic organ prolapse. This group included nine French gynecologic specialists with experience in the use of synthetic material who began working in 2000 on a standardized technique and material for the transvaginal treatment of prolapse. (Debodinance et al, 2004). Like the prior work with TVT, these pelvic surgeons worked on the development for what would become Prolift over many years of research and observation and study. Given the larger application and need to support various pelvic organs and provide level 1 and 2 support, Gynemesh PS mesh was chosen and it would ultimately be placed with arms passing through the sacrospinous ligament (SSL) for the Posterior Prolift and arcus tendinus fascia pelvis (ATFP) for the Anterior Prolift which had been established prolapse support structures for prior SSLF and paravaginal repairs.

Like the original Prolene mesh, Gynemesh PS is a macroporous Type 1 Prolene polypropylene mesh. It has a larger pore size, approximately 2.4 mm (2,400 microns), given the larger prolapse application and was cleared by the FDA for this indication in 2002. In this application it is a lightweight mesh weighing 43 g/m2 with noted flexibility and the ability to support the pelvic organs when cut to its configuration in the Anterior, Posterior and Total Prolift devices. The device is state of the art and the use of Gynemesh PS macroporous Prolene polypropylene mesh for prolapse repair was selected as it was the state of the art material for this

application. By the time of Prolift's release in March 2005, the macroporous Prolene polypropylene mesh had seven years follow up with the TVT demonstrating its long term safety and biocompatibility (Nilsson et al, 2004). Macroporous polypropylene was also the consensus graft material for prolapse treated abdominally (Nygaard et al, 2004).

TVM was studied in patients beginning in 2002 and by 2005 there were over 600 patients who had underwent TVM, an unheard of number compared to other prolapse products and studies at the time and it was well beyond industry standard and state of the art. (Debodinance et al, 2004; Cosson et al, 2005). A one year study of Gynemesh PS placed vaginally or abdominally was also presented at AUGS. (Lucente et al, 2004).

Specifically designed trocars were developed to provide access to the SSL and ATFP while ingenious cannula were developed and incorporated into the Prolift device which allowed smooth and atraumatic placement of the mesh without tissue dragging. The cannula also allowed mesh adjustment before removal allowing the user to take tension off the arms and place the mesh flat before deployment. The mesh could be trimmed to fit the specific patient as warranted. Various modifications in technique such as avoiding large incisions and T incisions reduced the rate of mesh exposure and the higher rate of exposure with concomitant hysterectomy was noted and presented in the early data and Prolift Surgical Technique Guide that accompanied the Prolift IFU. The higher rates of mesh exposure associated with concomitant hysterectomy have also been observed with abdominal sacral colpopexy.

Gynemesh PS and Prolift have been studied in several randomized controlled trials (RCTs) comparing it to native tissue repairs which establish that it is safe and efficacious, providing anatomic, subjective and quality of life improvements. Moreover, Prolift utilizing Gynemesh PS has been the subject of over 100 studies and has been studied more than any other surgical device used for prolapse surgery

An updated Cochrane Review involved 56 RCTs that evaluated 5,954 women following a search ending in August 2012 was published in 2013 (Maher 2013). Standard anterior repair was associated with more anterior compartment prolapse recurrence on examination than for any polypropylene (permanent) mesh repair (RR 3.15, 95% CI 2.50 to 3.96). Patient awareness of prolapse was also higher after the anterior repair as compared to polypropylene mesh repair (28% versus 18%, RR 1.57, 95% CI 1.18 to 2.07). However, the reoperation rate for prolapse was similar at 14/459 (3%) after the native tissue repair compared to 6/470 (1.3%)

(RR 2.18, 95% CI 0.93 to 5.10) after the anterior polypropylene mesh repair. Importantly, no differences in quality of life data or de novo dyspareunia were identified.

Since that time additional RCTs have been published concerning Prolift. The following was adapted from Table 1 of Jacquetin 2013 and updated with these data which show the anatomic superiority of using mesh and in particular Gynemesh PS and Prolift as compared to native tissue prolapse repair. Additionally, subjective improvements and quality of life scores are statistically significant in the Gynemesh and Prolift patients:

Study	Total pts./mesh pts. (n)	F/up (months)	Compartment	Mesh Anatomic Cure %	No mesh Anatomic Cure %	P value
Hiltunen 2007[#]	201/104	12	Anterior	93	62	<0.04
Sivaslioglu 2008[+]	90/45	12	Anterior	91	72	<0.05
Nieminen 2008[#]	201/104	24	Anterior	89	59	<0.05
Nguyen & Burchette 2008[%]	75/37	12	Anterior	87	55	<0.05
Carey 2009*	139/69	12	Anterior Posterior	81	65.6	0.07
Nieminen 2010[#]	201/104	36	Anterior	87	59	<0.0001
Withagen 2011**	190/93	12	All	90	55	<0.001
Altman 2011**	389/200	12	Anterior	82	48	0.008
Sokol 2011**	65/32	12	All	38	30	0.45
Halaska 2012**	168/85	12	All	83.1	60.6	0.003
El-Nazer 2012*	44/21	24	Anterior	95	70	<0.05
Svabik 2014**	70/36	12	All	97	35	<0.001
Dos Reis Brandão da Silveira 2015**	184/94	12	Anterior	86.4	70.1	0.019

[#] Utilized monofilament polypropylene mesh (Parietene light, Sofradim Co., Trevoux, France) to reinforce anterior colporrhaphy

+ Utilized monofilament polypropylene mesh (Parietene light, Sofradim Co., Trevoux, France) for site-specific anterior colporrhaphy

% Utilized Perigee Transobturator Prolapse Repair System (IntePro monofilament polypropylene mesh, AMS)

* Utilized Gynemesh PS

** Utilized Prolift

The largest study conducted on the outcomes of the Gynecare Prolift Anterior Prolift System was reported by Altman et al. This study randomized 389 women into a multicenter, RCT in which 389 women were randomized to either prolapse repair utilizing the anterior Prolift system (n=200) or native-tissue anterior colporrhaphy (n=189). This multi-center trial was conducted by 58 surgeons at 53 hospitals throughout Sweden, Norway, Finland, and Denmark (Altman et al, 2011). The primary outcome was a composite of objective and subjective measures: POP-Q stage 0 or 1 of the anterior vaginal wall (i.e., point Ba, which represents the most distal point of the anterior vaginal wall in relation to the hymen) and a negative response to the question, "Do you experience a feeling of bulging or protrusion in the vaginal area?" (question 16 on the UDI). Women who underwent anterior Prolift had a lower failure rate (39.2%) compared to native tissue repair (65.5%, $p < 0.001$). Pain and sexual function were not different between groups at any time point, and six subjects required surgery for mesh revision (3%).

There were no statistically significant differences seen in de novo dyspareunia, pelvic or genital pain (Table 4), change in vaginal length or sexual function as assessed by Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) (Table 2). Surgical reintervention to correct mesh exposure during follow-up occurred in 3.2% of Prolift patients in the Altman study. This finding is consistent with a study in 524 Prolift patients with three years follow up, which found the rate of mesh exposure needing surgical intervention was 2.5% (13/524) (De Landsheere 2012). Similarly, in a 75 patient study with a mean follow up of 54 months, mesh exposure occurred in four (5.3%) patients (Benbouzid 2012), with two requiring excision and the other two treated with estrogen. At last follow up, 64 (85.3%) patients were cured, with no prolapse recurrence.

Overall, studies comparing the use of mesh to native tissue repair in pelvic organ prolapse surgery approach vaginally, have shown better anatomical and similar-to-better functional outcomes. For example, in the study by El-Nazer et al. which used Gynemesh PS, statistically significant improvements were seen in subjective symptom assessments for urinary incontinence/urgency, voiding difficulty, vaginal pressure/bulge and sexual dysfunction symptoms, and notably, the improvements for voiding difficulty and vaginal bulge were significantly better for Gynemesh PS than the anterior colporrhaphy arm of the RCT. (El-Nazer et al, 2012, Table 4) Pain and dyspareunia were numerically but not statistically higher at 12 months with native tissue repair compared to Gynemesh PS. New onset dyspareunia was reported in 8.3% for the native tissue arm and 0% in the Prolift arm.

Another prospective RCT in 116 women at a median follow up of 28 months comparing tension free Gynemesh PS-reinforced anterior vaginal prolapse with anterior colporrhaphy at the time sacrospinous colpopexy and posterior fascial plication for the management of women with severe symptomatic pelvic organ prolapse (i.e. uterine or vaginal vault prolapse of stages III and IV) demonstrated significant improvements with Gynemesh PS. (Qatawneh et al, 2013). The overall objective success rates (in all compartments) were 79% (42/53) in the Gynemesh PS group and 62% (39/63) in the non-mesh group, and this difference was statistically significant in favor of the mesh group (p=0.043). The objective success rates in the anterior compartment were 85 % (45/53) in the Gynemesh PS group and 62 % (39/63) in the non-mesh group (p=0.006). Point Ba and Point C were significantly higher in the Gynemesh PS arm (p=0.004 and 0.024 respectively). Significantly fewer women underwent repeat surgery for recurrent prolapse in the Gynemesh PS group - three (6 %) patients in the Gynemesh PS group and 12 (19 %) in the non-mesh group(p=0.03). Subjective success and patient satisfaction were high with Gynemesh PS and trended in favor of the mesh group; subjective success rates were 89 % (47/53) in the Gynemesh PS group and 76 % (48/63) in the nonmesh group and mean patient satisfaction rates with the surgery were 84 % in the Gynemesh PS group and 76 % in the non-mesh group (p=0.08 for both outcomes). The development of a urinary tract infection, right-sided buttock pain (temporary sciatic neuralgia) and new-onset stress urinary incontinence were not significantly different between the two groups. The mesh exposure rate was 8 % with most exposures being asymptomatic.

More recently, several randomized trials have been performed comparing Prolift to native tissue vault repairs such as the SSLF (Halaska et al, 2012; Svabik 2014; da Silveira et al, 2014). These RCTs show statistically significant anatomic improvements versus native tissue vault repair. Also in the RCTs by Halaska and Svabik the POP-Q point C (top of vagina) was significantly higher postoperatively in the Prolift arm compared to native tissue. Significant improvements in subjective outcomes and quality of life were also seen overall in patients treated with Prolift.

Additionally in the da Silveira RCT, significant differences in PQoL scores at baseline and at 1- year follow-up were observed in each group. And, on between-group comparison, the treatment response was found better in the Prolift arm at 1-year follow-up as compared to native tissue (Table 5). This shows statistically significant improvements in quality of life for the patients who had Prolift over that in the native tissue arm. Halaska 2012, table 3 shows significant improvement for the Urinary Impact Questionnaire (UIQ), the Colorectoanal Impact Questionnaire

(CRAIQ), and the Pelvic Organs Prolapse Impact Questionnaire (POPIQ) scores and there was less improvement of bowel symptoms (CRAIQ) in the SSF group than in the mesh group. In Svabik 2014, which involved patients with levator ani avulsion injury, POPDI (Pelvic Organ Prolapse Distress Inventory), UDI (Urinary Distress Inventory) and CRADI (Colorectal Distress Inventory) questionnaire scoring significantly improved from baseline.

A retrospective cohort of anterior Prolift (n=40) versus anterior colporrhaphy (n=40) by Ignajatovic et al reported lower rates of anatomic failure with Prolift (11%) compared to native tissue repair (51%, p=0.004), with no differences in symptoms of urinary incontinence, quality of life, sexual function or sensation of vaginal bulge at 12 months. (Ignjatovic I et al, Obstet Gynecol Reprod Biol. 2010; 150(1):97-101).

Based upon a review of the literature, I have concluded that there is strong evidence to support the use of synthetic mesh augmentation compared to native tissue repair for vaginal repair of pelvic organ prolapse.

There was no overall difference in de novo dyspareunia or pelvic pain, sexual functioning by PISQ scores, or change in total vaginal length in these studies. In the Svabik RCT, there was an 8% mesh exposure rate for Prolift while in the SSLF arm, there was a 15% rate of granulation tissue leading to vaginal blood spotting. In Abed's SGS systematic review, erosion/exposure rates were 10% for synthetic and biologic grafts (range 0-29.7%) and wound granulation in 7% of synthetic grafts and 9% in biologic grafts (Abed 2011). 16 patients (20.8%) had mesh exposure in the Halaska 2012 RCT with only one-quarter symptomatic. Six patients underwent resection under general anesthesia and four with local anesthesia. Six exposures resolved with local estrogen. In the da Silveira RCT, there was a 20% rate of mesh exposure. There was a 7.4% extrusion rate for the SSLF group. Despite these differences, the Prolift group had significantly higher quality of life improvement and satisfaction was also very high. In the RCT conducted by Iglesia et al (Iglesia, 2010 / Sokol 2011), there was a 15% rate of Prolift mesh exposure compared to a 15% rate of suture erosion in the native tissue arm.

It is important to recognize that common surgical complications such as pain, dyspareunia, bleeding or adjacent organ injury are similar across surgical techniques, and not unique to those involving mesh implant. The risks of prolapse surgery can vary from minor to severe and are known to surgeons who are the intended users of the Prolift. All surgery including surgery to treat prolapse is per

se dangerous and requires due care. Surgeons are taught this in medical school, residency and further training and complications are known to occur with all surgeries. That is a fundamental tenet of surgery. There are numerous elemental, known risks of vaginal and prolapse surgery such as injury to organs, vessels, nerves and adjacent tissue, infection, bleeding, pain including dyspareunia and pelvic pain, wound complications, tissue contraction and scarring, voiding problems, recurrence, and the need for reoperation. Pelvic floor surgeons know of these risks from their basic surgical training and they are obvious to the intended user of Prolift given our surgical training and expected knowledge.

All of these risks have long been reported in the medical literature and are expected to be known by surgeon users. (Francis & Jeffcoate 1961; Lane 1962; Benson et al, 1996; Iglesia et al, 1997) Risks of vaginal and prolapse surgeries are also a part of the major gynecologic, urologic and urogynecologic textbooks and risks are also tested during training and are a part of specialty and subspecialty certification. For example, it is obvious to a pelvic floor surgeon who performs incontinence and prolapse surgeries that use of surgical instruments like a Prolift trocar can lead to organ, vessel and nerve damage. All prolapse and incontinence surgeries can lead to wound complications as earlier referenced such as granulation tissue, wound herniation, dehiscence, and suture, mesh and biologic graft erosion, which are obvious given our training and use of instruments and materials during surgery. They are analyzed and discussed in professional society analyses, reviews, guidelines and statements, as well as the FDA public health notice of 2008, the 2011 FDA advisory committee proceedings, and the FDA's 2013 statement concerning midurethral slings. Notably, the corresponding native tissue and suspension procedures do not have an IFU and Professional education like is present for the Prolift, which supplement all of the other sources of the surgeon's knowledge. The IFU and Professional education for the Prolift are clear, useful and adequate to describe the procedure and potential risks. Risks of vaginal and prolapse surgery are obvious to surgeons and as surgeons, we are expected to be aware of the risks in light of our education, training and experience.

Operative mesh revisions for vaginal exposures range from 3 – 8% across clinical studies and are manageable. This is typically the result of a breakdown or opening of the vaginal incision after surgery. In many cases, exposures can be treated with estrogen or the vagina can be reclosed over the mesh. However in some cases, the exposed portion of mesh is excised and the vaginal tissue closed, which is usually performed as an outpatient under local analgesia and light sedation.

As earlier noted, wound complications occur at similar and even higher rates with native tissue and suspension repairs. (Toglia 2008, Abed et al 2011; Yazdany 2010; Barber et al, 2014). My group published a study in a cohort of patients undergoing SSLS and reported a 36% suture-related complication rate at a mean time of 18.9 months with 25% of patients undergoing rate suture removal. Similarly, Yazdany 2010 found a 44.6% suture related complication rate that included a 36.1% rate of suture erosion with USLS. In the recent PFDN OPTIMAL randomized control trial, Barber et al reported 19.1% granulation tissue and 15.4% suture erosion rates for the USLS arm versus 14% granulation tissue and 17.2% suture erosion rates for the SSLF arm at 6 to 24 months follow up. In the Abed 2011 SGS Systematic Review , 110 studies reported on erosions with an overall rate of 10.3% (synthetic 10.3%; biological 10.1%) and 16 studies reported on wound granulation for a rate of 7.8% (synthetic 6.8%; biological 9.1 %).

While plaintiffs' experts claim that Prolift can lead to dyspareunia, it should be pointed out that baseline, postoperative and de novo dyspareunia are risks with all prolapse surgeries. These are well known and long described to surgeons (Francis & Jeffcoate 1961). The rates seen with Prolift and Gynemesh PS are comparable to alternative prolapse repair techniques that are based upon native tissue plication (Altman 2011; Ignjatovic 2010; Lowman 2007, Table 4 below):

TABLE 4
De novo dyspareunia after prolapse surgery

Dyspareunia	ASC N = 224 (148)[a] Handa et al[21]	SSLF N = 287 (106)[a] Maher et al[6]	USS N = 110 (34)[a] Silva et al[27]	APR N = 165 (81)[a] Weber et al[15]	Prolift N = 129 (57)[a]
Baseline (preop) dyspareunia (%)	40.5 (60/148)	Unknown	20.6 (7/34)	8.0 (6/81)	36.8 (21/57)
De novo (postop) dyspareunia (%)	14.5 (11/76)	36.1 (22/61)	25.9 (7/27)	19.0 (14/75)	16.7 (6/36)

[a] Number sexually active preop.

Lowman. Does the Prolift system cause dyspareunia? Am J Obstet Gynecol 2008.

Overall the earlier referenced RCTs with Gynemesh PS and Prolift show no differences in pelvic pain, dyspareunia, change in vaginal caliber or total vaginal length as compared to non-mesh, native tissue prolapse repair. Dietz and Maher conducted a meta-analysis of mesh and non-mesh prolapse studies, which documented no difference in post-operative dyspareunia, de novo dyspareunia or PISQ-12 scores (Int Urogynecol J. 2013 Nov; 24(11):1853-7). While Plaintiffs' experts make claims concerning contraction, tissue contraction and vaginal stenosis is a known risk with all POP surgeries as well as perineorrhaphy (Francis & Jeffcoate 1961; Carey 2009), and rates requiring treatment with Prolift are low.

In a group of over 500 Prolift patients with three years follow up, the rate of contraction needing surgical intervention was 0.4% (2/524) (De Landsheere 2012). It is important to recognize that the studies reviewed here report relatively few serious complications, with rates similar between mesh augmented and non augmented repairs.

In the most recent Cochrane Review by Maher et al published in 2016, on the subject comparing polypropylene transvaginal mesh repair to native tissue:

- Awareness of prolapse at one to three years was less likely after mesh repair (RR 0.66, 95% CI 0.54 to 0.81, 12 RCTs, n = 1614);
- Rates of repeat surgery for prolapse were lower in the mesh group (RR 0.53, 95% CI 0.31 to 0.88, 12 RCTs, n = 1675);
- There was no evidence of a difference between the groups in rates of repeat surgery for continence (RR 1.07, 95% CI 0.62 to 1.83, 9 RCTs, n = 1284);
- 8% of women in the mesh group required repeat surgery for mesh exposure;
- Recurrent prolapse on examination was less likely after mesh repair (RR 0.40, 95% CI 0.30 to 0.53, 21 RCTs, n = 2494);
- There was no evidence of a difference between the groups in rates of de novo dyspareunia (RR 0.92, 95% CI 0.58 to 1.47, 11 RCTs, n = 764).

(Maher et al, 2016). In summary, there is high quality evidence that the use of synthetic non absorbable mesh, such as Gynemesh PS and Prolift to suggest no difference for subjective outcomes such as sexual function at one year of follow up.

The accusations that vaginal mesh causes dyspareunia above and beyond the rates seen in prolapse surgery, as a whole, is not supported, by the substantial scientific data that has been reported and analyzed. Neither the Cochrane and SGS systematic reviews support these contentions: Studies reporting on dyspareunia following graft use were not consistent in reporting whether these incidence rates of dyspareunia are de novo or persistence of already existing pain. Overall, dyspareunia affected 9.1% of patients, with similar rates between biological and nonabsorbable synthetic grafts (9.6% and 8.9%, respectively). Of course, dyspareunia may also occur with native tissue prolapse repairs, and the RCTs do not show a risk that is significantly higher than what would be expected with native tissue repairs. The authors do not find any evidence to support the plaintiff experts' accusations for cancer, infection, mesh contracture, or other complications.

Overall, the data from these high quality randomized controlled trials and long term registries do not support the claims that Prolift places a women at a significant risk of long term, chronic complications or the need for reoperation as plaintiffs' experts suggest.

Another area of criticism has centered on the choice of Gynemesh PS polypropylene. However, the use of reinforcing materials in the surgical management of these disorders has increased significantly in the past 30-40 years within the field of female pelvic floor reconstruction. While both biologic and synthetic material have been proposed for this application, for the most part, the use of biologic xenografts and allografts has been shown to be unsatisfactory (Fitzgerald et al BJU, 1999; Huang, 2001; Fitzgerald 1999), and their clinical use has substantially declined since the introduction of synthetic mesh slings. Graft extrusion is still a recognized complication of biologic graft slings (Chung 2002) and pelvic organ prolapse grafts (Abed et al 2011).

Several clinical trials have evaluated the use of biologic graft in the treatment of pelvic organ prolapse. Overall, these trials do not support the use of biologic grafts, relative to native tissue repair. One RCT noted significantly higher anatomic failure rates after graft augmented repair compared to native tissue repair (Paraiso et al 2006). Other trials have also failed to demonstrate a benefit of using biologic grafts as well (Sung VW et al, Obstet Gynecol 2012; 119:125-33; Grimes CL et al, Obstet Gynecol. 2009; 114:59-65). The recent Cochrane Review did not find any benefits with the use of biologic grafts compared to native tissue prolapse repair. (Maher et al, 2016)

The use of synthetic absorbable mesh in the surgical management of pelvic organ prolapse has been explored as well, with two moderate quality RCTs demonstrating no benefit to the use of absorbable mesh (Weber AM et al, Am J Obstet Gynecol. 2001; 185:1299-304; Madhuvrata P et al, Obstet Gynaecol. 2011; 31:429-35). The use of Vypro (Prolene and Vicryl) was assessed by the French TVM surgeons and was found to not be well tolerated or feasible (Jacquetin et al, 2004). Although Ultrapro, which is comprised of Prolene polypropylene and an absorbable Monocryl component has been used in the Prolift +M device, similar rates of exposure (15%) was seen at 36 months follow up. (Milani et al, 2012). Additionally, a 9% rate of de novo dyspareunia at 3 years was also seen by Milani et al. Quemener et al, 2014 reported an 8% re-operation rate for 250 patients who underwent Prolift +M at a median follow-up duration of 20 months. When compared to de Landsheere et al's similar assessment of over 500 Prolift patients,

no statistical difference between the two groups for global rate of reinterventions for exposure, SUI or prolapse recurrence was found. (Table 3). A one year study of Prolift and Prolift +M demonstrated positive and equivalent improvements in sexual function as assessed by PISQ-12 questionnaires. (Bhati et al, 2012) The recent Cochrane Review does not support better outcomes or safety with the use of partially absorbable mesh over polypropylene mesh like Gynemesh PS which has demonstrable benefits. (Maher et al, 2016)

Therefore, many surgeons have focused on the use of permanent polypropylene synthetic implants to compensate for damaged tissue and in hopes of providing long term durable results.

Gynemesh PS is a type 1, macroporous, monofilament polypropylene mesh and has been repeatedly demonstrated to offer the desired mechanical properties of durability and elasticity as well as excellent host tolerability and lack of evidence of rejection. Type 1 macroporous mesh with pore size > 75 microns allows for infiltration by macrophages, fibroblasts, blood vessels in angiogenesis and collagen fibers (Amid 1997).

Some have raised concerns about the possibility of an adverse host tissue response to type 1 polypropylene mesh tape. These opinions are based largely upon studies involving animal models or studies involving abdominal hernia repairs. Studies that have specifically evaluated the pelvic floor tissue response are limited to small case series, and often are typically to a subset of subjects that have chronically extruded mesh implants. It is important to recognize that animal studies are not directly transferable to human subjects, and that individual tissue responses at different anatomic locations are likely to differ.

Plaintiff's experts have argued about the potential carcinogenesis of implanted pelvic floor mesh. After an extensive review of the existing literature, I have concluded that these assertions lack scientific validity. These opinions are founded upon a report from 1958, when Oppenheimer et al identified the development of various sarcomas in rats implanted with sheets of plastic film (Cancer 1958; 11:204–213). Of note, the latency times to cancer formation ranged from 7 months to two years in this study. Interestingly, in some previous animal models, it was noted that surface area, shape and surface morphology had an impact on the risk of sarcoma development, with perforated materials having lower risks than solid, flat films of material (McGregor et al, Eur J Cancer 2000; 36:307–313). More recent animal studies evaluating monofilament and multifilament polypropylene mesh implantation in the subcutaneous tissues of mice did not corroborate these findings,

with no sarcomas identified during two years of follow up (Witherspoon et al, Br J Surg 2004; 91:368–372). Despite the widespread use of synthetic mesh in surgical procedures in humans over the past 50 years, there have been few reports of malignancy formation after implantation with prosthetic materials. These concerns have recently been addressed by Moalli et al and it was concluded that polypropylene, which has been used extensively in humans for over five decades, is not associated with carcinogenesis. (Moalli et al, 2014). As stated in the AUGS/SUFU Frequently asked questions by providers- Mid-urethral slings for stress urinary incontinence "There is no compelling evidence supporting human malignant transformation related to polypropylene despite the millions of individuals implanted with various forms of this material span well over a half century world-wide." (AUGS-SUFU FAQs by Patients on Mid-urethral Slings for SUI March 2014). Type 1 macroporous, monofilament polypropylene has been found to be the most biocompatible biomaterial for use in the pelvic floor (Ford 2015).

With specific regard to synthetic midurethral slings and meshes used in pelvic floor support, there is no reliable scientific evidence to indicate that mesh induces malignancy. Several large observational series have now been published looking at synthetic mid urethral polypropylene slings. King et al reported on 2,361 patients who underwent synthetic sling placement, and found one case each of bladder and vaginal cancer for an incidence of 0.08%, with mean follow up of 42 months (Urology 2014; 84:789–792). In a more recent series, Linder et al discovered only 2 cases amongst 2,474 who underwent polypropylene midurethral sling placement (0.08%) with a mean follow up of 61.5 months (Int Urogynecol J. 2016 Feb 10. Epub ahead of print). In this study, 49 cancer diagnoses occurred before the date of sling placement. Thus the background rate of cancer in these patients was 2% (49 out of 2,474). This high background rate of cancer further demonstrates the lack of reliability in Plaintiffs' experts' position that polypropylene causes cancer in women when used for pelvic reconstruction. Notably, there are no epidemiologic data that show a statistically significant increased rate and risk of cancer with polypropylene midurethral slings and meshes used in pelvic floor support compared to the expected population level data. Additionally, the Mayo Clinic group found that no local cancers were detected among the 302 patients (12 % of the cohort) with more than 10 years' follow-up.

Both groups concluded that given the histology, location, and expected background incidence of these cancer, that there was no evidence of an association between mesh placement with subsequent local cancer formation. In order to establish an association, between polypropylene mesh and cancer formation, it must be

demonstrated by more than case reports (Goldman et al, Int Urogynecol J. 2016; 27:345-6.)

Another claim has been made that the Prolene mesh in Gynemesh PS is cytotoxic. This actually is based on in vitro testing that accompanied the TVT 510k submission. It is notable that this information was presented to the FDA within the context of available human data that showed clinical efficacy and safety. Notably, the FDA reviewed this anomaly and cleared the TVT. The overall clinical data do not show that the mesh is cytotoxic in humans. If it were the mesh would not incorporate into the tissues and instead it would lead to abundant necrotic tissue formation and rejection, which is not seen in the literature. The randomized controlled trials, cohort studies and systematic reviews show excellent efficacy, safety and tolerability, which is the opposite of what one would expect to see if the mesh were cytotoxic.

Another concern raised has been the possibility that the polypropylene mesh used in mid-urethral slings and pelvic organ prolapse degrades over time. Again, it can be pointed out that polypropylene, and specifically Prolene polypropylene, is a stable and well accepted biomaterial with an extensive use for over five decades as a biologic implant. These concerns seem to focus on reports that have detected "cracked surfaces" along portions of explanted synthetic mesh, visible only with very high scanning electron microscopy magnification, and the further hypothesis that these microscopic features could lead to adverse clinical outcomes. For example, the Clave et al paper reported surface cracking was observed in only one third of polypropylene monofilament explanted specimens that were available for analysis. However, according to the authors specific deteriorations correlating to implant material were not observed (Clave et al, 2010). The authors further acknowledge that they were unable to conform their hypotheses concerning potential degradation of PP include whether or not direct oxidation occurs in vivo. Additional limitations acknowledged were that they were unable to determine whether the mechanical properties were altered and they had not analyzed implants from non-pathologic states. In my opinion, the observations of surface cracking in a minority of specimens does not establish that degradation occurs and more importantly, that the mechanical and functional properties are in any significant way compromised. Finally, the authors state that they were unable to predict whether or not these changes could or do occur in non-pathologic states. Again, the opinions expressed by sub-specialty societies such as AUGS and SUFU have dismissed these concerns by pointing out that they are not supported by extensive peer reviewed literature related to polypropylene mesh repair (AUGS-SUFU FAQs by Providers on Mid-urethral Slings for SUI March 2014). Moreover, my analysis

of the data, including the numerous long term studies on TVT as well as with Gynemesh PS, leads me to conclude that the Prolene polypropylene does not degrade or if it did, that it has a clinically significant effect. Prolene polypropylene has been studied more than any other material for use as a sling and it is the best material as borne out by the clinical data discussed in this report.

Also, it has been suggested by plaintiffs' experts that Prolene mesh can result in chronic inflammation or infection. While some degree of a chronic host response to an implanted material is to be expected, there is no definitive scientific evidence to suggest that this effect is deleterious or clinically significant. None of the long term studies cited in this report support the Plaintiff experts allegations, and the metaanalyses and systematic reviews that I have referenced show that infection of the mesh is exceedingly rare. For example, in the Norwegian National Incontinence Registry, which included 4,281 women who had a TVT operation, the infection rate was 0.7% (Dyrkorn et al, 2010). I have personally implanted over 2,500 TVTs and have seen no mesh infection. Importantly, contamination does not equate to infection. Concerns that bacteria adhere to the TVT tape during implantation and lead to clinical infection is not supported by the broad base of high quality scientific papers on the worldwide TVT experience. (Ford Cochrane Review 2015) Overall the rate of infection with Prolift and Gynemesh PS is very low and is not higher than non-mesh prolapse repairs. In the three year study by De Landsheere, the rate of mesh infection leading to surgery was 0.2% (1/524). Even a study by one of plaintiffs' experts does not support this concern, as Klinge et al also reported in a rat model, that in vitro bacterial adherence occurs significantly less frequently with monofilament mesh compared to multifilament mesh and that the persistence of bacteria did not lead to a clinically higher rate of infection (Klinge 2002). In my experience, complications are largely user dependent and decrease with experience.

V. Summary

The use of graft augmentation in prolapse repair came as a necessity from the significant failure rates with native tissue repairs. These native tissue repairs may be complicated by dyspareunia, wound complications and granulation tissue formation in a similar manner to what occurs with graft-augmented repairs.

Gynemesh PS and the Prolift device is the most extensively studied mesh implant used in surgical procedures for pelvic organ prolapse in history. Numerous studies of varying level of scientific evidence support its clinical effectiveness and

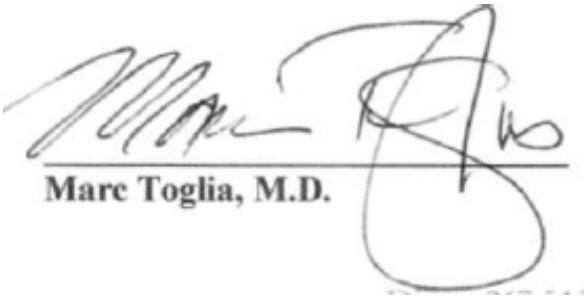
high level of patient satisfaction, as well as demonstrating superior anatomic cure to native tissue repair. It is less morbid and invasive than sacral colpopexy. No other surgical treatment for POP before or since has been subject to such extensive investigation. None of the Cochrane reviews or systematic reviews that have been published support the Plaintiff's safety or design allegations, although that is not to say that prolapse surgery is without risk.

Based upon a review of the literature, I have concluded that there is strong evidence to support the use of synthetic mesh augmentation compared to native tissue repair for vaginal repair of pelvic organ prolapse

It is important to recognize that the studies reviewed here report relatively few serious complications, with rates similar between mesh augmented and non augmented repairs. Most importantly, none of the long term clinical studies suggest that there are ongoing clinical concerns such as the development of cancer, clinically significant inflammatory complications or infections.

In summary, there is high quality evidence that the use of synthetic non absorbable mesh, such as Gynemesh PS and Prolift to suggest no difference for subjective outcomes such as sexual function at one year of follow up.

The issues of concern are not unique to Gynemesh PS and Prolift. They are a group of complications that are common to prolapse procedures. Complications such as dyspareunia, pelvic pain, and wound complications occur with equal frequency in native tissue procedures (Karram et al 2013; Dietz & Maher 2013; Toglia 2008; Barber et al 2015; Sokol et al 2011). Many of these risks decrease significantly as the user gains more experience. Overall, the data from these high quality long term studies do not support the claims that Prolift or Gynemesh PS places a women at a significant risk of long term, chronic complications or the need for reoperation as plaintiffs' experts suggest.



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